REMARKS

Claims 34, 39, 45-47, 56, 58, 62 and 65-73 are currently pending. Claims 56, 62 and 73 are independent.

Claims 32, 41, 42, 57, 59-61, 63 and 64 have been canceled by the present amendment. Applicants make no admission regarding the cancellation of these claims and reserve the right to pursue the subject matter of these claims in this application or in a continuing application.

Claims 34, 39, 45-47, 56, 58 and 62 are currently amended. Claims 56 and 62 have been amended to recite that the lock flush composition is biocompatible ***in a patient's bloodstream***. Each of claims 34, 39, 45-47 and 58 is a multiple dependent claim, and the only amendments have been to cancel certain claim dependencies to claims that have been canceled.

No new matter has been added. Applicant respectfully requests after entry of the amendment.

New Claims

New claims 65-73 have been added.

New claim 65 is independent and recites a lock flush composition ***consisting of*** at least one salt of ethylene diamine tetraacetic acid (EDTA) in a solvent, wherein the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a concentration of between 2.0% (w/v) and 8.0% (w/v), wherein the solvent consists of at least one of water, saline solution, or ethanol, wherein the lock flush composition has a pH of at least 9.5.

Support for new claim 65 may be found throughout the specification. New claim 65 is patentable over the cited art, as Fahim teaches multiple additional components, in addition to an EDTA salt in a solvent. Further, one skilled in the art would have no reason to modify

Fahim to consist only of an EDTA salt in a solvent. Accordingly, claim 65 is at least patentable over the cited art for this reason.

New claims 66-71 depend from claim 65. Support for new claims 66-71 may be found throughout the specification. New claims 66-71 are patentable over the cited art, at least for the reason new claim 65 is patentable.

New claim 72 depends from claim 65, and recites that the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a concentration of ***between 2.0% (w/v) and 6.0% (w/v)***. Support for new claim 72 may be found throughout the specification. New claim 72 is patentable over the cited art, at least for the reason new claim 65 is patentable. Further, the art does not teach or suggest the claimed concentrations.

New claim 73 depends from claim 65, and recites that the at least one EDTA salt comprises at least one of tri-sodium and tetra-sodium EDTA at a concentration of ***between 3.6% (w/v) and 4.4% (w/v)***. Support for new claim 73 may be found throughout the specification. New claim 73 is patentable over the cited art, at least for the reason new claim 65 is patentable. Further, the art does not teach or suggest the claimed concentrations.

Art Rejection

With regard to independent claims 56 and 62, the Office asserts that:

> the [alleged] intended use of the composition "wherein the lock flush composition is biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes", does not further limit the claim because the recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Official Action mailed 3 August 2010, page 5.

As discussed herein, the Fahim handwash is not biocompatible in a patient's bloodstream. The Office has asserted that Fahim is biocompatible because of the results of a dermal irritation test and ocular irritation test in the Examples of Fahim.

The sample tested in Fahim had a pH of about 7.5. In contrast, the claimed the lock flush composition has a pH of at least 9.5. The results of a dermal irritation test and an ocular irritation test with sample with a pH of 7.5 are not comparable to the results that would be obtained with a sample with a pH of 9.5. As pH is based on a logarithmic scale, there is a 100-fold difference in a pH of 7.5 compared to a pH of 9.5. Accordingly, it cannot be stated that Fahim teaches or suggest that a handwash at a pH of 9.5 is biocompatible with the epidermis and eye.

Even if the handwash of Fahim is considered biocompatible with the epidermis and eye[1], this does not mean that Fahim is biocompatible in a patient's bloodstream.

Biocompatible is defined as follows "the condition of being compatible with living tissue or a living system by not being toxic or injurious and not causing immunological rejection." *Merriam-Webster's Medical Dictionary*, 2002.

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[1] Applicants do no acquiesce to any conclusion the Office may have drawn from the tests of Fahim, including that the Fahim handwash is biocompatible for the epidermis and eye. For example, the tests for biocompatibility relied upon by Fahim are strictly related to the cosmetics and soap industry. The tests are specific to skin and eye exposure. The eye portion of the test is to test the *accidental* exposure to the eyes when washing with soaps or using cosmetics. They do not test for bloodstream contact. Further, the tests of Fahim do not provide reliable results. Fahim states he did not conduct the *required* 5 tests to actually establish bio-compatibility as **required** in the very source he relies on (Kay, 1962). One skilled in the art would recognize this is not a credible or reliable "teaching." Fahim states he **failed to do 80%** of required tests to claim biocompatibility, as such the results cannot show biocompatibility.

Biocompatibility with the bloodstream is ***different*** than biocompatibility with external contact with the body. This difference is explained below.

There is a clear difference in the effect a toxin may have when used externally to the body, such as on the skin or the eye, as compared to given direct access into the body via the bloodstream.

For example, in the cosmetic tests Fahim conducted, the first 48 hours were very toxic to the eye of the rabbit he tested. Fahim states the exposure caused conjunctivitis and opacity of the iris. Opacity of the iris is listed as the ***most severe*** of the possible toxic responses by Draize (cited by Fahim). Further, Fahim uses 0.1 ml for testing toxicity. A typical lock flush solution in a tube and catheter may be 20-70 times this amount.

Applicants have offered direct declaratory evidence, which is supported by independent research, including research sponsored and adopted by the U.S. government, relating to a key distinction for internal versus external biocompatibility. A declaration was provided by Dr. Stephen Olmstead, an internist, cardiologist and scientist, and Paul Ketteridge, a pharmacist and former drug consultant for the FDA, which recites that:

> Skin cleansers and other topical preparations meant for application on epidermal surfaces may employ active agents and excipients that would be toxic if ingested. For this reason, no medical practitioner or person skilled in the art of antimicrobials would ever find that a patent on a skin cleanser would teach anything obvious to the invention of an antimicrobial for oral or parenteral administration. ***An obvious example is that plain chlorine bleach, 3–6% sodium hypochlorite (NaClO), is an excellent antimicrobial. While it is irritating to the skin, contact with dilute solutions can be tolerated. However, ingestion of chlorine bleach is highly toxic causing corrosive tissue damage of the gastrointestinal track.***

Declaration of Olmstead & Ketteridge, paragraph 3 (emphasis added).

Regarding the individual components of the Fahim handwash -- triclosan, PCMX, and glutaraldehyde --the Office must recognize that each is not biocompatible when given direct access into the body via the bloodstream.

For example, triclosan is not biocompatible when given direct access into the body via the bloodstream:

> The EPA gives triclosan high scores both as a human health risk and as an environmental risk. Triclosan is a chlorophenol, a class of chemicals suspected of causing cancer in humans. Externally, phenols can cause a variety of skin irritations, but since they can temporarily deactivate sensory nerve endings, contact with it may cause little or no pain. ***Taken internally, even in small amounts, phenols [such as triclosan] can lead to cold sweats, circulatory collapse, convulsions, coma, and death***. Reports suggest that triclosan can combine with chlorine in tap water to form chloroform gas (PMID 15926568), which the EPA classifies as a probable human carcinogen. Triclosan was the subject of a United Kingdom cancer alert. Triclosan reacts with the free chlorine in tap water to produce lesser amounts of other compounds, like 2,4-dichlorophenol (PMID 15926568). Most of these intermediates convert into dioxins upon exposure to UV radiation (from the sun or other sources). Dioxins are extremely toxic and are very potent endocrine disruptors. Triclosan has been shown to disrupt testosterone biosynthesis in testicular Leydig cells (PMID 18655822).

Declaration of Olmstead & Ketteridge, paragraph 4 (emphasis added).

Further, the Office must recognize that PCMX is not biocompatible when given direct access into the body via the bloodstream:

> Fahim teaches 4-chloro-3,5-dimethyl phenol (Chloroxylenol, also known as parachlorometaxylenol, or PCMX) as a component. ***While chloroxylenol is used as an antimicrobial in soaps, shampoos, and sprays, it has never been approved for oral or parenteral administration. Despite its topical use, chloroxylenol may be a skin, eye or respiratory tract irritant and is considered harmful if swallowed.*** … This again underscores that there is nothing in Fahim that makes it relevant to any bactericidal application except topical uses. The PAN Pesticides Database maintained by the Pesticide Action Network North America … notes that Chloroxylenol is highly corrosive and causes caustic eye, skin, mouth and gastrointestinal injuries. Ingestion can result in nausea, vomiting, diarrhea, hypotension, myocardial failure, pulmonary

> edema, neurological changes, liver and renal toxicity, methemoglobinemia, and hemolysis. It is readily apparent that this component of Fahim cannot be sterilized, placed in a vial, and administered to humans. No reasonable practitioner skilled or even unskilled in the art would even think about doing this.

Declaration of Olmstead & Ketteridge, paragraph 5 (emphasis added).

Moreover, the Office must recognize that glutaraldehyde is not biocompatible when given direct access into the body via the bloodstream. See Declaration of Olmstead & Ketteridge, paragraphs 7-11. In particular, glutaraldehyde has been shown to be highly toxic when allowed to contact the bloodstream. See Declaration of Olmstead & Ketteridge, paragraphs 9-11 (Glutaradehyde has a median lethal dose that places glutaraldehyde as highly toxic according to Occupational Safety and Health Administration).

Thus, understanding that there is a clear difference in the effect a toxin may have when used externally to the body, such as on the skin or the eye, as compared to given direct access into the body via the bloodstream, the Office must consider the above declaratory evidence, which is supported by independent research, including research sponsored and adopted by the U.S. government. The evidence shows that even if the handwash of Fahim is recognized as biocompatible with the epidermis and eye[2], the

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[2] Applicants do no acquiesce to any conclusion the Office may have drawn from the tests of Fahim, including that the Fahim handwash is biocompatible for the epidermis and eye. For example, the tests for biocompatibility relied upon by Fahim are strictly related to the cosmetics and soap industry. The tests are specific to skin and eye exposure. The eye portion of the test is to test the *accidental* exposure to the eyes when washing with soaps or using cosmetics. They do not test for bloodstream contact. Further, the tests of Fahim do not provide reliable results. Fahim states he did not conduct the *required* 5 tests to actually establish bio-compatibility as **required** in the very source he relies on (Kay, 1962). One skilled in the art would recognize this is not a credible or reliable "teaching." Fahim states he **failed to do 80%** of required tests to claim biocompatibility, as such the results cannot show biocompatibility.

handwash of Fahim must be considered as not being biocompatible in a patient's bloodstream.

The handwash of Fahim is not biocompatible in a patient's bloodstream, at least because, if the handwash of Fahim were to come into contact with the bloodstream, the handwash of Fahim would not be compatible internally in the body of a living organism, but would be toxic and injurious and cause immunological rejection.

A composition that is toxic and injurious and causes immunological rejection, as the handwash of Fahim is when in a patient's bloodstream, is not biocompatible. A biocompatible composition requires that composition is "compatible with living tissue or a living system by not being toxic or injurious and not causing immunological rejection." *Merriam-Webster's Medical Dictionary*, 2002.

Accordingly, the handwash of Fahim is not biocompatible in a patient's bloodstream. This is the result of a clear structural difference between the handwash of Fahim and the claimed composition. The Office asserts that if the prior art structure is capable of performing the [alleged] intended use, then it meets the claim. Official Action mailed 3 August 2010, page 9. While applicants again stress that "biocompatible" is not an intended use, even if "biocompatible" can be so interpreted, the case law establishes that, if the prior art structure is not capable of performing the [alleged] intended use, then is it does not meet the claim. See In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997); In re Swineheart, 169 USPQ 226 (CCPA 1971); and In re Pearson, 181 USPQ 641 (CCPA 1974).

In fact, the case law is clear that an intended use recitation may establish a patentable distinction if the recitation "define[s], indirectly at least, some characteristic not found in the old composition." In re Pearson, 181 USPQ 641, 644 (CCPA 1974). The claim recitation that the "lock flush composition is biocompatible in a patient's bloodstream," directly, or at least indirectly, establishes some characteristic not found in Fahim (as discussed *supra*).

Further, in the Official Action, the Examiner asserts that "[t]he arguments are not commensurate in scope with instant claims because instant claims do not recite administration of instant compositions orally or parenterally." Official Action mailed 3 August 2010, page 8. However, as established above, the arguments are commensurate in scope with a claim that requires that the lock flush composition be biocompatible in a patient's bloodstream. The Office has relied upon the information in Fahim related to ***external*** contact (skin and eyes), but not ***bloodstream*** contact. Applicants have provided the relevant information related to internal contact (e.g., in the bloodstream). Accordingly, Applicants have established that the handwash of Fahim is not biocompatible in a patient's bloodstream.

Accordingly, the rejection is respectfully requested to be withdrawn.

Further, applicants assert that one skilled in the art would not have reason to use a lock flush solution that is biocompatible in a patient's bloodstream at the claimed pH of claims 56 and 62 (pH at least 9.5). Instead, one skilled in the art would have had reason to design or buffer a lock flush solution that is biocompatible in a patient's bloodstream to be essentially at a physiological pH of ~7.365. There is no reason for one skilled in the art to modify the solutions of the cited art to have a pH of at least 9.5 when such a solution is a lock flush solution that is biocompatible in a patient's bloodstream. That is, any reference relied upon by the Office that allegedly teaches a lock flush solution at a pH near the physiological pH of ~7.365 is not a reference the renders the present claims obvious, without an express reason for one skilled in the art to modify such to a pH of at least 9.5.

Accordingly, the Office is requested to withdraw the rejection of independent claims 56 and 62, and claims 34, 39, 45-47 and 58 depending therefrom.

Conclusion

Applicants traverse the rejection for at least the reasons discussed above. However, applicants make no admissions from a lack of a response to any of the Office's assertions.

In the event that there are any questions concerning this amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned attorney so that prosecution of the application may be expedited.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.20(d) and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

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